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Docket No.: 203348US0CONT

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF:	:
Yusuke AMINO, et al.	: GROUP ART UNIT: 1625
SERIAL NO: 09/809,197	: EXAMINER: OH, T.V.
FILED: MARCH 16, 2001	: ALLOWED: APRIL 8, 2003

FOR: N-ALKYLASPARTYL DIPEPTIDE ESTER COMPOUNDS

FAX RECEIVED
NOV 0 6 2003
PETITIONS OFFICE

PETITION TO WITHDRAW FROM ISSUE UNDER 37 CFR §1.313(c)(2)

COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, VA 22313-1450

SIR:

Further to the Issue Fee paid on June 23, 2003, Petitioners respectfully request the Office to Withdraw the present allowed application from Issue under the provisions granted Petitioners by 37 CFR §1.313.

37 CFR §1.313(c) states:

> "Once the issue fee has been paid, the application will not be withdrawn from issue upon petition by the applicant for any reason except: . . . .(2) Consideration of request for continued examination in compliance with §1.114; . . . ."

Concurrent with the present Petition, Applicants have filed a Request for Continued Examination in compliance with §1.114. A copy of the request for continued examination is attached for the convenience of the Petition's Office.

If prosecution of an application is closed and a Petition under 37 CFR §1.313 is granted, an applicant may request continued examination under 37 CFR §1.114 by filing a submission and a fee. Petitioners respectfully filed the appropriate fee set forth in 37 CFR

§1.17(e) required by 37 CFR §1.114. Further, Petitioners respectfully filed an appropriate submission under 37 CFR §1.114(c).

37 CFR §1.114(c) states:

> "A submission as used in this section includes, but is not limited to, an information disclosure statement, an amendment to the written description, claims, or drawings, new arguments, or new evidence in support of patentability . . . . ."

Petitioners have timely filed with the Request for Continued Examination, and an Information Disclosure Statement, and a list of related cases, which qualifies as an appropriate submission as set forth in 37 CFR §1.114(c). A copy of the Information Disclosure Statement is enclosed for the convenience of the Petition's Office. Accordingly, Petitioners have timely filed a Request for Continued Examination in compliance with §1.114 as set forth above. In accordance with 37 C.F.R. § 1.17(h) the required fee for filing this 37 C.F.R. § 1.313 Petition is included herewith and, as such, Applicants have fulfilled the requirements for filing a Petition under 37 CFR §1.313.

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It is requested that the Petition be GRANTED and the references cited on the concurrently filed Information Disclosure Statement be considered.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.

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PLEASE CALL US AT (703) 413-3000 IF THE MESSAGE YOU RECEIVE IS INCOMPLETE OR NOT LEGIBLE

TO	Wan Laymon (NAME)	November 6, 2003 (DATE)	
	U.S.P.T.O. (COMPANY/FIRM)	703-308-6916 (FAX #)	
	NUMBER OF PAGES INCLUDING COVER: 18	CONFIRM FAX: ☐ YES ■ NO	
FROM	Vincent K. Shier, Ph.D. (NAME)	203348US0CONT (OUR REFERENCE)	
	703-412-6461 (DIRECT PHONE #)	09/809,197 (YOUR REFERENCE)	

MESSAGE

Per my telephone conversation with Mrs. Frances Hicks the following courtesy copies are enclosed:

Date-stamped Filing Receipt dated November 5, 2003
PTO Transmittal Letter
Petition to Withdraw from Issue Under 37 §1.313(c)(2)
Request for Continue Examination (RCE) Transmittal
Information Disclosure Statement
List of Related Cases
Cited Pending Application (1)

Best regards,

Vincent K. Shier, Ph.D.

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PETITIONS OFFICE

Unless otherwise indicated or obvious from the nature of the transmittal, the information contained in this facsimile message is attorney privileged and confidential information intended for the use of the individual or entity named above. If the reader of this message is not the intended recipient or the employee or agent responsible to deliver it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this communication is strictly prohibited. If you have received this communication in error or are not sure whether it is privileged, please immediately notify us by telephone and return the original message to us at the above address via the U.S. Postal Service at our Expense. Thank You.

Dept.: C

OSMM&N File No. 203348US0CONT By: SGB/VKS/scs

Serial No. 09/809,197

In the matter of the Application of: Yusuke AMINO, et al.

For: N-ALKYLASPARTYL DIPEPTIDE ESTER COMPOUNDS

Due Date: N/A

The following has been received in the U.S. Patent Office on the date stamped hereon:

- Credit Card Form for $130.00
- Dep. Acct. Order Form
- PTO Transmittal Letter
- Petition to Withdraw From Issue Under 37 CFR §1.313(c)(2)
- Copy of RCE Transmittal filed November 5, 2003
- Copy of Information Disclosure Statement filed November 5, 2003
- Copy of List of Related Cases filed November 5, 2003

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OBLON
SPIVAK
McCLELLAND
MAIER
&
NEUSTADT
P.C.

ATTORNEYS AT LAW

Docket No.: 203348US0CONT

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

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RE: Application Serial No.: 09/809,197
Applicants: Yusuke AMINO, et al.
Filing Date: March 16, 2001
For: N-ALKYLASPARTYL DIPEPTIDE ESTER COMPOUNDS
Group Art Unit: 1625
Examiner: OH, T.V.
Allowed: April 8, 2003

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NOV 0 6 2003
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SIR:

Attached hereto for filing are the following papers:

Petition to Withdraw from Issue Under 37 CFR §1.313(c)(2); Copy of RCE Transmittal filed November 5, 2003; Copy of Information Disclosure Statement filed November 5, 2003; Copy of List of Related cases filed November 5, 2003

Our credit card payment form in the amount of **$130.00** is attached covering any required fees. In the event any variance exists between the amount enclosed and the Patent Office charges for filing the above-noted documents, including any fees required under 37 C.F.R 1.136 for any necessary Extension of Time to make the filing of the attached documents timely, please charge or credit the difference to our Deposit Account No. 15-0030. Further, if these papers are not considered timely filed, then a petition is hereby made under 37 C.F.R. 1.136 for the necessary extension of time. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.

Stephen G. Baxter, Ph.D.
Registration No. 32,884

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#24

Docket No.: 203348US0CONT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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IN RE APPLICATION OF: Yusuke AMINO, et al.

SERIAL NO: 09/809,197 GAU: 1625

FILED: March 16, 2001 EXAMINER: OH, T.V.

FOR: N-ALKYLASPARTYL DIPEPTIDE ESTER COMPOUNDS

REQUEST FOR CONTINUED EXAMINATION (RCE) TRANSMITTAL

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

SIR:

This is a request for Continued Examination (RCE) under 37 C.F.R. §1.114 of the above-identified application.

Submission required under 37 C.F.R. §1.114

Previously Submitted:

☐ Consider the amendment(s)/reply under 37 C.F.R. §1.116 previously filed on

☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on

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NOV 0 6 2003
PETITIONS OFFICE

Enclosed:

☐ Amendment/Reply

☐ Information Disclosure Statement (IDS)

■ Other: Information Disclosure Statement, List of Related Cases, Cited Pending Applications (1)

FEES	RATE	CALCULATIONS
☐ Suspension of action on the above-identified application is requested under 37 C.F.R. §1.103(c) for a period of months.	$130.00	$0.00
■ RCE Fee required under 37 C.F.R. §1.17(e)	$770.00	$770.00
☐		$0.00
☐		$0.00
TOTAL OF ABOVE CALCULATIONS:		$770.00
☐ REDUCTION BY 50% FOR FILING AS SMALL ENTITY		$0.00
TOTAL:		$770.00

☐ A check in the amount of _____ is enclosed

■ Credit card payment form is attached to cover the fees in the amount of **$770.00**

■ Please charge any additional fees for the papers being filed herewith and for which no check or credit card payment is enclosed herewith, or credit any overpayment to Deposit Account No. 15-0030. A duplicate copy of this sheet is enclosed.

■ If these papers are not considered timely filed by the Patent and Trademark Office, then a petition is hereby made under 37 CFR 1.136, and any additional fees required under 37 CFR 1.136 for any necessary extension of time may be charged to Deposit Account No. 15-0030. A duplicate of this sheet is enclosed.

Respectfully Submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.

Stephen G. Baxter, Ph.D.
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#20

Docket No. 203348US0CONT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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IN RE APPLICATION OF: Yusuke AMINO, et al.

SERIAL NO: 09/809,197 GAU: 1625

FILED: March 16, 2001 EXAMINER: OH, T.V.

FOR: N-ALKYLASPARTYL DIPEPTIDE ESTER COMPOUNDS

INFORMATION DISCLOSURE STATEMENT UNDER 37 CFR 1.97

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

SIR:

Applicant(s) wish to disclose the following information.

REFERENCES

☐ The applicant(s) wish to make of record the references listed on the attached form PTO-1449. Copies of the listed references are attached, where required, as are either statements of relevancy or any readily available English translations of pertinent portions of any non-English language references.

☐ A check or credit card payment form is attached in the amount required under 37 CFR §1.17(p).

RELATED CASES

■ Attached is a list of applicant's pending application(s) which may be related to the present application. A copy of the claims and drawings of the pending application(s) is attached.

☐ A check or credit card payment form is attached in the amount required under 37 CFR §1.17(p).

CERTIFICATION

☐ Each item of information contained in this information disclosure statement was first cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this statement.

☐ No item of information contained in this information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application or, to the knowledge of the undersigned, having made reasonable inquiry, was known to any individual designated in 37 CFR §1.56(c) more than three months prior to the filing of this statement.

DEPOSIT ACCOUNT

■ Please charge any additional fees for the papers being filed herewith and for which no check or credit card payment is enclosed herewith, or credit any overpayment to deposit account number 15-0030. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.

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LIST OF RELATED CASES

Docket Number	Serial or Patent Number	Filing or Issue Date	Inventor/ Applicant
218254US0CONT	10/177,205	04/08/02	KAWAHARA, et al.
203348US0CONT*	09/809,197	03/16/01	AMINO, et al.

*Present Application; listed for information

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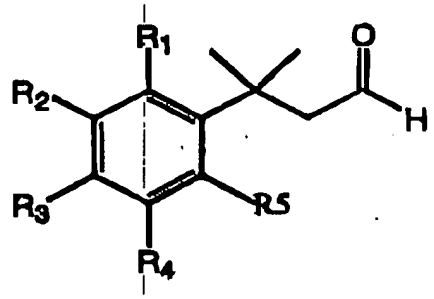
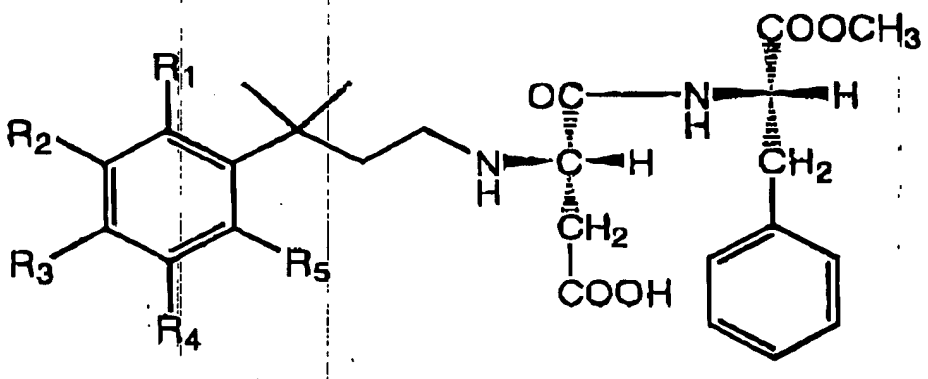
WHAT IS CLAIMED IS:

1. A process for producing aspartyl dipeptide ester derivative represented by formula (2), which comprises:

reductively alkylating aspartame with the aldehyde represented by formula (1):



(1)



(2)

wherein R_1, R_2, R_3, R_4 and R_5 are independently selected from the group consisting of a hydrogen atom, a hydroxyl group, an alkoxy group having 1 to 3 carbon atoms, an alkyl group having 1 to 3 carbon atoms, a benzyloxy group and a

Related Pending Application
Related Case Serial No: 10/117,205
Related Case Filing Date: 04.08.02

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hydroxyalkyloxy group having 2 or 3 carbon atoms,

wherein R_1 and R_2, or R_2 and R_3 form a methylene dioxy group, and

provided that in formula (2), any one of R_1, R_2, R_3, R_4 and R_5 does not represent a benzyloxy group.

2. The process as defined in claim 1, wherein R_3 is a methoxy group, and R_1, R_2, R_4 and R_5 are hydrogen atoms.

3. The process as defined in claim 1, wherein R_3 is a hydroxyl group, and R_1, R_2, R_4 and R_5 are hydrogen atoms, and in formula (1) R_3 is a hydroxyl group or a benzyloxy group.

4. The process as defined in claim 1, wherein R_2 is a methoxy group, R_3 is a hydroxyl group, and R_1, R_4 and R_5 are hydrogen atoms, and in formula (1) R_3 is a is a hydroxyl group or a benzyloxy group.

5. The process as defined in claim 1, wherein R_2 is a hydroxyl group, R_3 is a methoxy group, and R_1, R_4 and R_5 are hydrogen atoms, and in formula (1) R_2 is a is a hydroxyl group or a benzyloxy group.

6. The process as defined in claim 1, wherein R_1 is a hydroxyl group, and R_2, R_3, R_4 and R_5 are hydrogen atoms, and in formula (1), R_1 is a hydroxyl group or a benzyloxy group.

7. The process as defined in claim 1, wherein R_1 is a hydroxyl group, R_3 is a methoxy group, and R_2, R_4 and R_5 are hydrogen atoms, and in formula (1) R_1 is a hydroxyl group or a benzyloxy group.

8. The process as defined in claim 1, wherein R_1 is a hydroxyl group, R_3 is a methyl group, and R_2, R_4 and R_5 are hydrogen atoms, and in formula (1) R_1 is a hydroxyl group or a benzyloxy group.

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9. The process as defined in claim 1, wherein R_2 and R_3 are combined to represent a methylene dioxy group, and R_1, R_4 and R_5 are hydrogen atoms.

10. The process as defined in claim 1, wherein R_2 is a methyl group, R_3 is a methoxy group, and R_1, R_4 and R_5 are hydrogen atoms.

11. The process as defined in claim 1, wherein R_2 is a methyl group, R_3 is a hydroxyl group, and R_1, R_4 and R_5 are hydrogen atoms, and in formula (1) R_3 is a hydroxyl group or a benzyloxy group.

12. The process as defined in claim 1, wherein R_2 is a hydroxyl group, R_3 is a methyl group, and R_1, R_4 and R_5 are hydrogen atoms, and in formula (1) R_2 is a hydroxyl group or a benzyloxy group.

13. The process as defined in claim 1, wherein the reductive alkylating is conducted in the presence of hydrogenation catalyst.

14. The process as defined in claim 13, wherein said hydrogenation catalyst is palladium carbon or platinum carbon.

15. The process as defined in claim 1, wherein the reductive alkylating is conducted in a solvent of an alcohol or a water-containing alcohol.

16. A process for producing

3-(3-hydroxy-4-methoxyphenyl)-3-methylbutylaldehyde, which comprises:

converting a carboxyl group in 3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyric acid to a formyl group.

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17. The process as defined in claim 16, wherein said 3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyric acid is produced by converting a halogen atom in 3-(3-halogeno-4-methoxyphenyl)-3-methylbutyric acid to a hydroxyl group.

18. The process as defined in claim 17, wherein said 3-(3-halogeno-4-methoxyphenyl)-3-methylbutyric acid is prepared by reacting 2-halogenoanisole with 3-methylcrotonic acid.

19. The process as defined in claim 17, wherein the halogen atom is a chlorine atom or a bromine atom.

20. The process as defined in claim 18, wherein the reacting of 2-halogenoanisole with 3-methylcrotonic acid comprises reacting in the presence of an acid.

21. The process as defined in claim 16, wherein said converting a carboxyl group into a formyl group comprises reducing a carboxylic acid to an aldehyde; or converting a carboxyl group into a hydroxymethyl group and converting the hydroxymethyl group into a formyl group.

22. A process for producing N-[N-[3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, which comprises:

reductively alkylating the 3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyl

aldehyde obtained by the process of Claim 16 with aspartame

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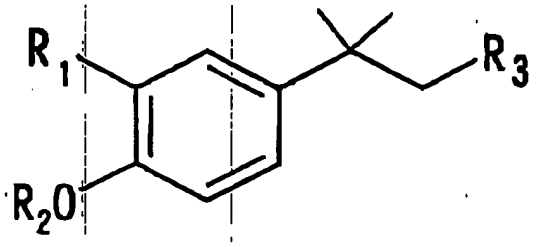
23. A process for producing N-[N-[3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, which comprises;

reductively alkylating 3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyl aldehyde with aspartame.

24. A compound of formula (3):



(3)

wherein R_1 is selected from the group consisting of a hydroxyl group, a halogen atom and a lower alkyloxy group having 1 to 4 carbon atoms, R_2 is a lower alkyl group having 1 to 4 carbon atoms, and R_3 is selected from the group consisting of a carboxyl group, a formyl group and a hydroxymethyl group,

provided that the compounds where R_1 is a chlorine atom or a bromine atom, and R_3 is a formyl group are excluded.

25. A compound selected from the group consisting of

3-(3-hydroxy-4-methoxyphenyl)-3-methylbutylaldehyde;

3-(3-chloro-4-methoxyphenyl)-3-methylbutyric acid;

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3-(3-bromo-4-methoxyphenyl)-3-methylbutyric acid;

3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyric acid; and

3-(3-hydroxy-4-methoxyphenyl)-3-methyl-1-butanol.

26. A process for producing N-[N-[3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyl]-L- α -aspartyl]-L-phenylalanine 1-methyl ester, which comprises:

subjecting N-[N-[3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyl]-L- α -aspartyl]-L-phenylalanine 1-methyl ester containing impurity to crystallize the compound.

27. The process as defined in claim 26, wherein said N-[N-[3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyl]-L- α -aspartyl]-L-phenylalanine 1-methyl ester containing impurity is obtained by reductively akylating aspartame and 3-(3-hydroxy-4-methoxyphenyl)-3-methylbutylaldehyde or a derivative thereof.

28. The process as defined in claim 26, wherein said impurity is one or more compounds selected from the group consisting of aspartame, an aspartame derivative, a peptide derivative, an amino acid, an amino acid derivative, an aldehyde and an aldehyde derivative.

29. The process as defined in claim 26, wherein a solvent used in the crystallization is selected from the group consisting of methanol, ethanol, isopropyl alcohol, acetone, methyl ethyl ketone, methyl isobutyl ketone, methyl acetate, ethyl acetate, propyl acetate, isopropyl acetate, butyl acetate, tetrahydrofuran, acetonitrile toluene, mixtures thereof; and mixtures thereof with water.

30. The process as defined in claim 26, further comprising removing said impurity from said N-[N-[3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyl]-L- α

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-asparty]-L-phenylalanine 1-methyl ester by extracting said impurity with a solvent.

31. The process as defined in claim 30, wherein said solvent is selected from the group consisting of toluene, diethyl ether, chloroform, dichloromethane, hexane, ethyl acetate, propyl acetate, isopropyl acetate and butyl acetate.

32. A crystal of N-[N-[3-(3-hydroxy-4-methoxyphenyl) -3-methylbutyl]-L- α -asparty]-L-phenylalanine 1-methyl ester, which exhibits peaks of diffractive X-ray in at least diffraction angles of 8.3° , 19.5° and 21.2° (2 θ , CuK α ray) when determined by powder X-ray diffractometry.

33. A sweetening composition comprising the crystal of N-[N-[3-(3-hydroxy-4-methoxyphenyl)-3-methylbutyl]-L- α -asparty]-L-phenylalanine 1-methyl ester as defined in claim 32 and a carrier or bulking agent.

34. A food or drink comprising the crystal as defined in claim 32 as an effective ingredient.

35. A process for sweetening a food or drink, comprising

adding the crystal as defined in claim 32 to a food, a beverage, or an intermediate product used for making the food or beverage, in an amount sufficient to sweeten said food or drink.

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ABSTRACT OF THE DISCLOSURE

The present invention relates to a method of manufacturing aspartyl dipeptide ester compounds, which can be used as sweeteners.

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Fig. 1